

STATUS REVIEW
FLUOROCHEMICALS IN BLOOD
5/22/79, PGG

- On May 30, 1978, 3M informed Du Pont of findings of organic fluorocarbons in blood of employees exposed to long-chain perfluoro surface-active materials. Organic fluoride blood levels of 1 to 71 ppm were found. Higher blood levels were associated with operations where airborne mists or dusts generated were in range of 48-81 ppm. 3M reports that some trace level of organic fluorine in humans is apparently normal, i.e. less than 1 ppm.

- Du Pont Program and Status

<u>Item</u>	<u>Status</u>
● Communication	
1. Inform affected C.W. employees of 3M information.	Complete 6/27/78
● Toxicity	
1. Haskell 10-Day Subacute Feeding Tests for MPD-5004 (homolog mixture of ammonium perfluoroalkyl carboxylates); perfluoroalkyl methacrylates (ZFM, TLF-1837); "Teflon" CSF Carpet Protector (TLF-4113-D); Zonyl BA (Telomer B Alcohol, TLF-1847); Zonyl FSC (TLF-3635C); Zonyl FSN (TLF-4714C); Zonyl FSD (TLF-3176); Zonyl Tela (Telomer A, TLF 4187).	Complete
2. Analysis of rat blood	Done for rats fed Zonyl FSN and Zony BA.
● Medical Program	
1. Review all current operations and industrial hygiene controls to insure that the potentials for exposures are properly controlled.	Complete
2. Identify all employees who currently work or have worked jobs in which there is or was potential for exposure to fluorochemicals.	Complete
3. Review the medical records of all such persons still employed by Du Pont, looking for consistent or unusual health occurrences or trends.	Complete

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- | | <u>Status</u> |
|--|-------------------------------------|
| 4. Obtain blood fluorochemical levels on persons who have never had potential for occupational exposure to fluorochemicals to establish background levels for a baseline. | Complete |
| 5. Obtain blood fluorochemical levels on representative employees with various potentials for exposures to various fluorochemicals. | Complete for 55 c
199 employees. |
| 6. Review the physical findings of the workers examined for consistent or unusual health occurrences or trends. | Complete |
| 7. If the period of potential exposure has been of sufficient duration and there is a sufficient number of employees, an epidemiologic study of the mortality of the cohort identified may be considered. A determination can be made of the likelihood of having a meaningful study after the number of previously exposed employees is determined. | To be decided |

● Program Cost to Date	Total	\$149,400
1. Toxicity Testing	MR-3089	17,000
	MR-3187	27,400
	Total	\$ 44,400
2. Blood Analysis (Additional blood analysis, ~\$500 each)		\$105,000

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CHAMBERS WORKS
FLUOROchemicals IN BLOOD STUDY

- (1) RESULTS OF STUDY - LEVELS OF FLUORINE IN THE BLOOD OF
CHAMBERS WORKS EMPLOYEES. (INORGANIC AND LOW VOLATILITY
ORGANIC FLUORINE)
- (2) INDUSTRIAL HYGIENE SURVEY
- MANUFACTURE OF TELOMER B ALCOHOL
 - MANUFACTURE OF ZEPER® FLUOROMONOMER, ZONYL® FSN, RP,
FSE, FSP, UR

R. D. RICHARDSON/AMB
18 MAY 1979

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ORGANIC FLUORINE IN BLOOD

GROUP (SAMPLE SIZE)

PPM ORGANIC FLUORINE*

3M DATA

GENERAL POPULATION (106)

0.002 TO 0.13
[0.02]**

PLANT OFFICE WORKER

0.01 TO 0.06

PLANT WORKER - GENERAL

0.13 TO 1.18

PLANT WORKER - LONG

SERVICE IN F/C AREA

NEWER PLANT

0.9 TO 9.1

OLDER PLANT

5.9 TO 71

DU PONT DATA

WILMINGTON CONTROL GROUP (25)

(23 OF 25) 0 - 0.38 ***
[0.094]

CHAMBERS WORKS GROUP (55)

(54 OF 55) 0 - 0.37 ****
[0.15]

CONCLUSIONS

- CHAMBERS WORKS EMPLOYEES DO NOT HAVE ELEVATED LEVELS OF ORGANIC FLUORINE IN THEIR BLOOD AS WAS REPORTED FOR 3M WORKERS.
- THE MEAN VALUE FOR CHAMBERS WORKS EMPLOYEES WAS SLIGHTLY HIGHER THAN THE WILMINGTON CONTROL GROUP [0.15 VERSUS 0.094], BUT ALL VALUES ARE CONSIDERED TO BE "NORMAL" (<1 PPM) EXCEPT ONE VALUE IN THE WILMINGTON CONTROL GROUP (10.6 PPM).

* BY DIFFERENCE BETWEEN
TOTAL AND INORGANIC FLUORINE

*** EXCEPT 2 VALUES 10.6;
0.78

** [MEDIAN VALUES]

**** EXCEPT 1 VALUE 0.89 PPM

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CHAMBERS WORKS FLUOROchemicalS COHORT

- CHAMBERS WORKS EMPLOYEES WERE IDENTIFIED WHO
 - (1) HAVE HAD JOB ASSIGNMENTS WITH POTENTIAL FOR EXPOSURE
 - (2) ARE STILL ACTIVE OR ARE READILY AVAILABLE ON SITE
- BLOOD SAMPLES TAKEN AT REGULARLY SCHEDULED PHYSICAL EXAMINATION

<u>JOB ASSIGNMENT</u>	<u>LOCATION</u>	<u>NUMBER IDENTIFIED</u>	<u>NUMBER CHECKED TO DATE</u>	<u>(%)</u>
R & D	JACKSON LAB. TECHNICAL LAB.	50	18	(36)
DEVELOPMENT MANUFACTURING	SPEC. CHEM. WEST	36	6	(17)
MANUFACTURING	SPEC. CHEM. EAST	84	26	(31)
	OTHER	29	5	(17)
		<u>199</u>	<u>55</u>	(28)

- INFORMAL CHECK WITH SUPERVISION INDICATED THAT GROUP (55) SAMPLED WAS REPRESENTATIVE OF COHORT (199).

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CONCLUSIONS - INDUSTRIAL HYGIENE SURVEY

A) TELOMER B ALCOHOL AND ZFM MANUFACTURE

- 1) ENVIRONMENTAL MONITORING DATA SUGGESTED CONDITIONS IN THE MANUFACTURING FACILITIES TO BE NORMALLY $<5 \text{ mg/m}^3$ TBA (8 HRS.). HOWEVER, EXCURSIONS TO RAISE THIS LEVEL TO 30 TO 40 mg/m^3 TBA (8 HRS.) HAVE BEEN OBSERVED ON MULTIPLE OCCASIONS.
- 2) ADDITIONAL ENVIRONMENTAL MONITORING REQUIRED TO IDENTIFY EXPOSURE SOURCES AND DEFINE POTENTIAL EXPOSURE LEVELS.
(IN PROGRESS)
- 3) MOST PROBABLE EXPOSURE SOURCES ARE DRUMMING AND ~~DEDRUMMING~~ FACILITIES, AND TO A LESSER EXTENT SAMPLING EQUIPMENT AND PROCEDURES.
- 4) DRUMMING, ~~DEDRUMMING~~ AND SAMPLING FACILITIES ARE OF A LOW STANDARD FOR CONTAINMENT BY ENGINEERING CONTROLS, (NOT ENCLOSED, NO LOCAL VENTILATION)
- 5) A CONTRIBUTING FACTOR IS THAT THE FACILITIES ARE ENCLOSED IN A BUILDING. PROMPT ELIMINATION OF PROCESS LEAKS AND - MAINTAINENCE OF VENTILATION IS ESSENTIAL.

B) TELOMER B ALCOHOL USE AREAS

LIMITED, AVAILABLE, ENVIRONMENTAL DATA SUGGEST THE POTENTIAL FOR EXPOSURE TO TBA (AND ZONYL® FSN) TO BE LOW.

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RECOMMENDATIONS

- 1) DISCONTINUE PROGRAM TO DETERMINE FLUORINE IN BLOOD,
- 2) ADVISE EMPLOYEES THAT BLOOD ANALYSIS PROGRAM HAS BEEN DIS-
CONTINUED DUE TO UNIFORMLY FAVORABLE RESULTS.
- 3) UPGRADE FACILITIES, IF REQUIRED, TO MEET HASKELL LABORATORY
EXPOSURE LIMIT GUIDELINES WHEN THESE ISSUE.

18 MAY 1979

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SUMMARY OF SUBACUTE TESTS WITH FLUOROCHENICALS

Compound	Report #	(mg/kg/day)	Mortality	Observations at 14 Days	Observations at 28 Days	(mg/kg) A.D.	(mg/kg) O.D.
TIF-2654	216-68	2250	0/5	↓ liver weight degenerative liver changes reversible histologic kidney changes mild gastroenteritis	pernated ↓ in severity ↓ in severity		
"Zonyl" RP	244-71	2250	0/6	↓ liver weight reversible histologic liver changes	returned to normal pernated	1100	
"Zonyl" RP, ammonium salt	245-71	2200	0/6	↓ liver weight reversible histologic liver changes	returned to normal pernated	2250	
"Zonyl" RP, ammonium salt of low ionizing	246-71	2200	0/6	↓ liver weight reversible histologic liver changes	pernated with only slight recovery pernated		
"Zonyl" RFA	157-78	90 45	6/10 0/10	reversible histologic changes in: GI tract, spleen thymus, bone marrow liver, testis	returned to normal good but incomplete recovery pernated with only slight recovery		421
"Zonyl" FSN	718-78	4470	0/10	reversible histologic spleen, bone marrow and thymus changes ↓ liver weight	returned to normal pernated		11,792
"Zonyl" FSC	720-78	200	0/10	no compound-related effects	no compound-related effects	1000	
"Zonyl" FSP	721-78	1400	0/10	↓ liver weight	partial recovery		>25,000
"Zonyl" TEIA	744-78	5000	0/10	↓ liver weight ↓ spleen and thymus weights necrosis of hemopoietic cells in spleen, bone marrow and thymus necrosis of germ cells with ↓ sperm production	partial recovery returned to normal nearly complete recovery pernated	>25,000	
Fluoromannomer 1837	747-78	3400	3/10	↓ liver weight ↓ erythropoietic foci in spleen	partial recovery returned to normal		
"Teflon" CSF	778-78	5000	0/10	reversible histologic liver changes	returned to normal		
Perfluoromethyl carboxylic acid, ammonium salt	44-79	300 150	9/10 3/10	↓ liver weight reversible histologic changes in: hemopoietic system, liver, kidney and G.I. tract non-reversible testicular damage	partial recovery pernated		
"Zonyl" BA	52-79	3400 1700 850	8/10 10/10 4/10	↓ liver weight histologic liver changes reversible histologic changes in several organs histologic testicular changes	partial recovery partial recovery returned to normal partial recovery	11,000	

BEST COPY AVAILABLE

Ninety-Day Feeding Study with "Zonyl" RP in Rats, Report #190-65

Dietary levels: 100, 500 or 2500 ppm for 15 days adjusted to 100, 1000 and 5000 ppm for 75 days

Observations: slightly decreased erythropoietic activity in spleen

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ORGANIC FLUOROCOMPOUNDS IN BLOOD

In May, 1978, 3M informed Du Pont of findings of organic fluorocompounds in blood of employees exposed to long-chain perfluoro-surface active materials. 3M reported airborne contaminant levels up to 81 ppm in their operations and organic fluorine blood levels of 1 to 71 ppm for exposed workers. 3M reports that some level of organic fluorine in humans is normal, i.e. equal to or less than 1 ppm.

Chambers Works makes functional equivalents to the 3M fluorosurfactants and plant employees were informed of the 3M findings in June 1978. Also a program was initiated to define exposure potential in the Chambers Works fluorocompound manufacturing and use operations, review the medical records of employees assigned to these operations, determine organic fluorine levels in the blood of such employees and to gather additional toxicity information on selected plant fluorocompounds. Program results are summarized below:

- Airborne contaminant monitoring results show that the highest potential for employee fluorocompound exposure to be in the manufacturing facilities. Eight hour time weighted average measurements ranged from <0.3 ppm (5 mg/m³) to 2 ppm (40 mg/m³). The drumming, dedrumming and sampling operations are major contributors to exposures above 0.3 ppm. Engineering control programs to reduce contaminant emissions from these sources is underway.
- Blood samples were taken from a representative sample of exposed employees and analyzed for organic fluorine. The mean organic fluorine value for Chambers Works employees was slightly higher than the Wilmington control group (0.15 ppm versus 0.094 ppm) but all values for exposed employees were less than 1 ppm. This program has been discontinued.
- A review and comparison of the medical records of active fluorocompound exposed plant employees with a control group showed no adverse health effects. However, while the difference is not statistically significant, the number of employees with abnormal liver function tests was notably higher in the exposed group (6 compared to 1). Medical surveillance will be continued with study update December, 1979.

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10-day subacute feeding tests carried out by Haskell showed compound related non-reversible effects for three of the eight fluorocompounds tested. Non-reversible liver and testes effects were noted in rats fed 4,470 mg/kg/day Zonyl FSN and 850 mg/kg/day Zonyl BA. Decreased sperm production was found in rats fed 5,000 mg/kg/day Zonyl Tela. The need for further toxicity testing is being studied.

A meeting is being arranged through Haskell Laboratory to inform 3M of the results of our program.

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E. I. DU PONT DE NEMOURS & COMPANY
INCORPORATED
WILMINGTON, DELAWARE 19898

CHEMICALS, DYES AND PIGMENTS DEPARTMENT

S. W. Doye
B. C. McKusick
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F. J. Marascia, CW
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R. M. Shepherd, PP&R
H. Serenbetz, Elas.
W. J. Raines, PP&R

Final
6/21

PERSONAL & CONFIDENTIAL

June 20, 1979

TO: MEETING ATTENDEES

FROM: P. G. GILBY

5/22
FLUOROCHEMICALS IN BLOOD
5/22/79 MEETING SUMMARY

This letter is to summarize discussions and decisions reached in the subject meeting. It was agreed that:

<u>Item</u>	<u>Responsible for Coordination</u>
● The Chambers Works program to determine organic fluorine blood levels will be discontinued.	--
● Chambers Works employees will be informed of the results and discontinuance of the blood analysis program.	R. Richardson
● Followup will be done in the Wilmington control group employee whose blood sample was analyzed at 10.6 ppm organic fluorine.	Dr. J. C. Bonnett (additional blood sample has now been submitted for analysis)
● Medical records review study of Chambers Works exposed and control group will be updated December 1979. Update will be limited to tabulation of abnormal liver function tests.	R. Richardson to submit updated tabulation to P. G. Gilby for transmission to Dr. S. Pell.

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ItemResponsible for Coordination

- Blood analysis will be done for employees having potential for exposure to 3M's FC-143 at Washington Works. PP&R will submit samples week of 6/18/79 to G. H. Patterson, CD&P, Jackson Laboratory for analysis. R. M. Shepherd, PP&R
- Engineering control programs to reduce Telomer B Alcohol airborne contaminant levels during drumming, dedrumming and sampling will be defined and projects initiated. R. Richardson
- Acceptable airborne contaminant exposure limits recommendations will be requested for Telomer B Alcohol (Zonyl BA), Telomer A (Zonyl Tela) and ZFM. W. Darnell (Request to Haskell submitted 6/12/79)
- The need, if any, for (1) further toxicity testing of selected fluorochemicals, (2) MSDS revisions and (3) customer notifications will be determined. R. E. Read
- A meeting will be set up with 3M to review Du Pont toxicity, blood and health information. F. E. French will coordinate through B. McKusick, Haskell

Discussion Summary

- Haskell completed 10-day subacute feeding tests and issued reports for the eight fluorochemicals submitted by CD&P for testing. Of the materials tested, compound related non-reversible liver and testes effects were noted in rats fed 4,470 mg/kg/day Zonyl FSN and ~850 mg/kg/day Telomer (Zonyl) BA. Decreased sperm production was found in rats fed 5,000 mg/kg/day Zonyl Tela.
- The medical records of 221 active Chambers Works employees known to have potential for fluorochemical occupational exposure were reviewed and compared to a control group. The control group (221 employees) was randomly selected from Chambers Works employees and matched as to sex, age and A.S.D. No adverse health effects were noted. However, while the difference is not statistically significant ($P < 0.05$), the number of employees with abnormal liver function tests was notably higher in the exposed group (6 compared to 1). Continued surveillance is warranted.

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- Blood samples were taken from a representative sample (55) of the Chambers Works exposed group and analyzed for organic fluorine. Du Pont Wilmington employees (25) having no potential for fluorochemical occupational exposure were used as the control group to establish base line levels. The mean value for Chambers Works employees was slightly higher than the control group (0.15 versus 0.094 ppm organic fluorine), but all values are considered to be normal (≤ 1 ppm) except one 10.6 ppm value found in the Wilmington control group. A second blood sample from this individual will be taken and analyzed. Additional blood analysis of Chambers Works employees is not warranted in view of the low values found.
- An industrial hygiene survey of selected Chambers Works fluorochemical manufacturing and use facilities was carried out. Fluorochemical exposure potential was found to be low in the use facilities. Airborne contaminant levels in the manufacturing facilities were normally 45 mg/m^3 (0.26 ppm), 8 hr. TWA. However, levels up to 40 mg/m^3 (2.1 ppm), 8 hr. TWA were measured and additional monitoring is being done to better define exposure sources. Most probable exposure sources are drumming, dedrumming and sampling operations (facilities are not now enclosed and have no local exhaust ventilation.) Engineering control programs to reduce airborne contaminants from these operations are being developed and projects will be initiated to improve these facilities.
- 3M's FC-123 fluorosurfactant is used at Spruance (TF) and Washington Works (PP&R). PP&R will submit employee blood samples for analysis. Textile Fibers have not yet reached a decision on whether or not blood analysis is warranted for their operations.

For additional information, see attached meeting charts.

PGG/bam
Att.

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Meeting Attendees:

J. C. Breckenridge
F. E. French
H. E. Hiestand
R. N. Knowles
W. H. Darnell
S. B. Cupp
L. Percival, PP&R
A. A. Wright, TF
J. C. Bonnett, ER
R. D. Richardson, CW
R. E. Read, Jackson Lab
G. H. Patterson, Jackson Lab
G. L. Thayer, Jackson Lab
H. J. Trochimowicz, Haskell
P. W. Schneider, Haskell

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